Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

August 7, 2003

Dear Colleague:

The August 8, 2003 issue of the *Morbidity and Mortality Weekly Report* (*MMWR*) contains an article entitled "Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection." The article revises the Centers for Disease Control and Prevention (CDC) and the American Thoracic Society (ATS) treatment recommendations for latent tuberculosis infection (LTBI) to indicate that the 2-month regimen of rifampin plus pyrazinamide (RZ) should generally not be offered.

The following is key background information:

- Studies in HIV-infected persons documenting the safety and efficacy of the RZ regimen for the treatment of LTBI led the ATS and CDC, in April 2000, to recommend this regimen for the treatment of LTBI. However, in October 2000, CDC received a report of a patient who died while receiving RZ. To investigate this event, CDC initiated surveillance for such adverse events and undertook a study to estimate their frequency.

- From October 2000 to June 2003, a total of 48 cases of confirmed RZ-associated severe liver injury were reported to CDC; 11 were fatal, including 2 known to be HIV-infected.

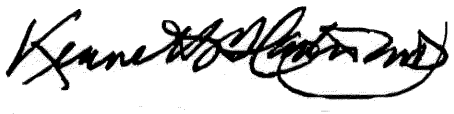
- To estimate the incidence of RZ-associated severe liver injury and provide more precise data to guide treatment for LTBI, CDC collected data from cohorts of patients in the United States who received RZ for the treatment of LTBI from January 2000 to June 2002. This survey found high rates of hospitalization and death from liver injury associated with the use of RZ.

- In May, June, and July 2003, CDC presented the surveillance data, survey results, and recent published studies of RZ-associated liver injury and hospitalization to several groups of national experts, including the ATS, Infectious Diseases Society of America (IDSA), the American College of Chest Physicians, and the Food and Drug Administration (FDA). After reviewing all these data and the experts' opinions, ATS and CDC (with IDSA endorsement) revised their original recommendation to advise that the RZ regimen should generally not be offered.

The response of CDC in identifying patients with adverse effects and issuing alerts to the medical community led to a rapid decline in reports of serious adverse effects; however, such events have continued to occur. Although we are recommending against the use of the RZ regimen, **we continue to strongly support the treatment of LTBI as a key component of CDC's efforts to eliminate tuberculosis**. Fortunately, other regimens for the treatment of LTBI are safe and effective. The preferred regimen is isoniazid (INH) for 9 months; alternatives are INH for 6 months or rifampin for 4 months. It is important to note that the recommendation against the use of RZ for treatment of LTBI does not apply to the appropriate use of rifampin and pyrazinamide in multidrug regimens for the treatment of persons with active TB disease.

Copies of this report may be viewed on the Internet at http://www.cdc.gov/mmwr/. If you have any questions or need additional information, please contact the National Center for HIV, STD, and TB Prevention's Office of Communications at 404-639-8890.

Sincerely,



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